REMARKS

Claims 1-33, 40, 59, and 70 were previously cancelled. Claims 41 and 61 are currently cancelled. Claims 34-38, 42, 44-48, 52-57 and 64-68 were previously withdrawn. Applicants reserve the right to file continuation or divisional applications directed toward the cancelled or withdrawn subject matter. Claims 39, 49, 51, 58 and 69 are currently amended. Support for the amendments can be found throughout the specification, specifically at page 2, lines 6-7 and the claims as originally filed. No new matter has been added. Claims 39, 41, 43, 49-51, 58, 60-63, 69 and 71-74 are currently under consideration.

Rejection Under 35 U.S.C. §112, First Paragraph--Enablement

Claims 39-42, 43, 49-51, 58, 60-63, 69, and 71-74 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The Examiner states that the specification "...while being enabling for use of *Tupaia belangeri* infected with HIV-1 or HBV in the claimed method for developing a therapeutic procedure, does not reasonably provide enablement for the use of any *Tupaia* species or for other human pathogens." Office Action page 3.

35 U.S.C. §112, first paragraph, requires that a specification enable one skilled in the art to make and use the claimed invention. A specification fails to meet this requirement if the specification fails to provide sufficient information regarding the claimed subject matter to enable a skilled artisan to make and use the claimed invention. "However, to comply with 35 U.S.C. §112, first paragraph, it is not necessary to 'enable one of ordinary skill in the art to make and use a perfected, commercially viable embodiment absent a claim limitation to that effect.' CFMT, Inc. v. Yieldup Int'l Corp., 349 F.3d 1333, 1338, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003)." (MPEP §2164). To determine if sufficient information is provided, one must inquire whether the claimed invention can be practiced without undue experimentation. MPEP §2164.01. That some experimentation may be required is not fatal because the issue is whether the experimentation is undue. In re Vaeck, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991).

Applicants respectfully disagree with the Examiner's rejection and assert that the claims are fully enabled. However, solely in an effort to promote prosecution, claims 39 and 49 have been amended to recite that the human viral pathogen is HIV 1 or HIV 2. As quoted above, the Examiner clearly acknowledges that the specification is enabled for HIV. Office

Action page 3.

The Examiner states on page 4 of the Office Action that "The claims encompass the use of any *Tupaia* species as an animal model for infection with any human viral pathogen." The specification notes three separate viral pathogens (HBV, HCV and HIV) as being almost exclusively infective in humans. The fact that these pathogens are infectious in *Tupaia belangeri* argues for a remarkable conservatism in *Tupaia* that extends from when there was common ancestor shared by humans and Tupaia. Although there is no description of tests performed on other species of *Tupaia*, the fact that such widely separately species (Homo sapiens and *Tupaia belangeri*) have a shared genetic characteristic (infectability) makes it likely that this characteristic would also be found among kindred species of the *Tupaia* genus.

The Examiner states that the claims cover any Tupaia species infected with any human viral pathogen. Office Action page 4. Applicants respectfully assert that this statement is overdrawn. The list of viruses encompassed by the claim language is narrower than what is asserted by the Examiner. For instance, rather than "any human viral pathogen", amended claims 39 and 49 are limited to HIV 1 or HIV 2 or a human retrovirus, and claims 58 and 69 are directed toward viruses that induce secondary clinical manifestations. Therefore, only a subset of human viral pathogens is covered by the claims. The Examiner states that no guidance is given for determining susceptibility to viral pathogens. Office Action page 4. The specification clearly described methods for determining susceptibility to HBV and HIV. Other studies have been carried out previously in *Tupaia* for other human viral pathogens such as HSV I and II (Darai et al., 1978 J. Inf Dis 137; 221-226), HCV (Xie et al., 1998 Virology 244 513-520) and human rotavirus (Pang et al., 1983 Chin Med J (Engl) 96; 85-94). Thus, methods to evaluate susceptibility of *Tupaia* to infection by a given viral pathogen are well understood by one skilled in the art. However, solely in the interest of furthering prosecution, claims 39 and 49 have been amended by importing several of the limitations of claim 41 as well as specifying that the retroviruses are HIV 1 or HIV 2. The same receptors (CCR5 and CXCR4) are present on both HIV 1 and HIV 2 (Hill et al., 1997 J Vir 71; 6296-6304) such that successful infection by HIV 1 indicates that HIV 2 will also be capable of infection by *Tupaia.*

The Examiner states on page 5 of the Office Action that "...genetic modification may be used to render a Tupaia animal susceptible to infection by any single human viral antigen." Such means are known to the skilled artisan and, therefore, do not require teaching in the

specification. For example, nucleic acids coding for virus receptors have been used to create transgenic mice strains that acquire infectability by otherwise human restricted viruses (Browning et al., Proc. Nat. Acad. Sci USA 94; 14,637-14,641 for HIV receptors; Ren and Racaniello 1992 J Vir 66; 296-304 for poliovirus receptors; Horvat et al., 1996 J. Vir 70; 6673-6681 for measles receptors; Zhang and Racaniello 1997 Virology 235; 293-301 for Echovirus receptors). However, this point is not relevant as this extra step is not a necessary part of the method of the pending claims. This step would not be required for HCV, HIV, and for some of the viruses that involve secondary manifestations (which include HCV, HIV, and HBV).

The Examiner discusses on page 5 of the Office Action problems associated with a suitable animal model. While it may be true that Lewis describes ideal characteristics, but for suitability as an animal model, utility may still be found despite inadequacies that do not allow an exact mirroring of the human condition. Even in the case of HIV, previous studies of various animal models have shown characteristics that differentiate them from the course of a true human HIV infection. However, these models may still be used as investigatory tools of various aspects of HIV disease. Thus, the development of alternative models may still provide an improvement over the use of previously described animal models.

Applicants therefore assert that there would be no undue experimentation needed for development of the Tupaia as an animal model. Administration of the infectious agent is beneficial in use in an animal model. Any further investigation into the other parameters would be necessary only for the purposes of establishing the particular strengths and weaknesses of Tupaia as an animal model, i.e., the degree to which Tupaia resembles a human infection for a particular viral pathogen. These evaluations would consist of standard testing methodologies well known to one of skill in the art and would be derived from known manifestations in a human subject.

Applicants also disagree with the Examiner's characterization of the scope of the claims as evidenced on page 5 of the Office Action: "Given the very broad scope of the claims, which includes genetic manipulations to enhance viral susceptibility..." As stated above, genetic manipulation is not a necessary part of the claimed methods. In many cases this manipulation would not be required. This technique would be necessary in only isolated cases where Tupaia is not a natural host for a particular virus; for instance, transformation into a susceptible host when a further step is undertaken (i.e., generating a transgenic animal

with a viral receptor by means of standard techniques).

Therefore, Applicants respectfully contend that the claims as currently amended, drawn to a method for developing a procedure in an animal system comprising infecting Tupaia with a human viral pathogen wherein the pathogen is HIV 1 or HIV 2 are fully enabled by the present specification. As discussed above, "The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation." *United States v. Telectronics, Inc.*, 857 F.2d 778, 785 (Fed. Cir. 1988). Withdrawal of the rejection of claims 39-42, 43, 49-51, 58, 60-63, 69 and 71-74 is respectfully requested.

Rejection Under 35 U.S.C. §112, First Paragraph—Written Description

Claims 39-41, 43, 49-51, 58, 60-63, 69 and 71-74 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The Examiner states that

> The claims are directed to the use of a Tupaia species as an animal model for infection with a human viral pathogen and methods for developing a therapeutic procedure.
>
> The claims encompass the use of any Tupaia species as a model for any human viral pathogen in the claimed methods. However, the specification only discloses two animal model systems.

Office Action page 6.

Under 35 U.S.C. §112, first paragraph, a specification must describe the invention with sufficient detail so that one of ordinary skill in the art would conclude that the inventor had possession of the claimed invention. MPEP (Rev. 6, Sept. 2007) §2163; *Lockwood v. American Airlines, Inc.*, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997).

Generally, "there is a strong presumption that an adequate written description of the claimed invention is present when the application is filed. [Citation omitted]." MPEP §2163. It is the Patent Office's burden to overcome this presumption and establish that one skilled in the art would not recognize that the inventor had possession of the claimed invention because, for example, the recited elements that are not conventional in the art or known to one of ordinary skill in the art and are not described in the specification. MPEP §2163; *In re Alton*, 76 F.3d 1168, 1175-76 (Fed. Cir. 1996) (holding that the Patent Office, "must provide

reasons why one of ordinary skill in the art would not consider the description sufficient.").

Applicants respectfully disagree with the Examiner's assertion that the claims are directed to the use of Tupaia in "any human viral pathogen". The Examiner cites to a wide variety of human viral pathogens on page 6 of the Office Action. However, most of the cited pathogens are not applicable to the subject matter of claims 39, 49, 58, and 69. The first two claims relate only to HCV, HIV 1, and HIV 2, while the latter two claims refer to viral pathogens that exhibit secondary manifestations.

On pages 6 and 7 of the Office Action, the Examiner states that "The instant specification only deals with two viral pathogens and their infectivity on a single species of Tupaia." As discussed above, HIV-2 can utilize the same receptors as HIV-1 such that successful infection by HIV-1 makes it highly likely that HIV-2 will also share this same characteristic. It was known in that art at the time of filing the instant application that HCV can infect Tupaia. However, it was not known whether HCV infection of Tupaia duplicated secondary manifestations that are the hallmark of human infection by both HBV and HCV. The parallels between the HBV and HCV self-destructive immune responses in humans make it very likely that this would continue to be paralleled in Tupaia infections and, as such, it has been predicted that HCV would have secondary disease manifestations.

The Examiner further states that "The specification does not disclose any process developed or derived from any animal model as set forth in the claims." Office Action page 7. Contrary to the Examiner's assertions, Example 2 specifically describes a therapeutic process (oral tolerization) that was developed using the Tupaia as an animal model. Decreases in secondary disease manifestations were noted and commented upon in this Example. The present application teaches the use of an animal model that would be suitable for procedures to be developed by the user. Once given this tool, one skilled in the art would have the ability to use this tool.

Applicants provide for the Examiner's convenience a copy of the following articles: Xie, (1998); Zhao et al., (2000) and Xu, (2007).

The Examiner states on page 8 of the Office Action that Applicants have provided no evidence pertaining to viruses grown in mouse cells. Applicants assert that it is known in the art that many retroviruses have extremely wide host ranges such that they are infective towards humans as well as mice. It was a reasonable conjecture that retroviruses of this type would also be able to infect Tupaia since they lacked any high level of selectivity towards

hosts. The growth of retrovirus in mouse cells may be later used for infections of human subjects is a widely used genetic therapy protocol. It is also well known that the host range of retroviral vectors is dependent upon the nature of the receptor that is involved in a binding event. Thus, a retrovirus with an ecotropic env may have the ability to transduce a few related species, such as mouse and rat, while an amphotropic retrovirus will have the ability to transduce a wide variety of species including mouse, rat, hamster, rabbit, mink, cow, cat, dog, monkey, human, and even chicken (reviewed in Miller 1996 Proc. Nat. Acad. Sci. USA 93; 11,407-11,413). It is thus not surprising that in a review of tropisms, the host range of some of these retroviruses is summarized as "mammals" (Table 1 in Manet et al., 2005 Oncogene 24; 6016-6025). Thus, it is hard to imagine that many varieties of retrovirus would not have the ability to infect Tupaia.

The Examiner acknowledges on page 9 of the Office Action that human disease symptoms would be known for a given viral pathogen, but then states that it would be unknown which pathogen would be held in common with infection of Tupaia. Ascertaining particular manifestations in the Tupaia model would simply require adaptation of the same tests used in humans, thus incurring the use of standard tests. The viral pathogens influenza, measles and mumps are not encompassed by the current claims as: a) they are not HCV, HIV 1, or HIV 2 as required by claims 39 and 49 and b) they do not induce secondary disease manifestations as required by claims 58 and 67.

The amended claims are clearly described in the specification such that one of skill in the art would conclude that Applicants had possession of the claimed invention. Applicants respectfully request withdrawal of the rejection of claims 39-41, 43, 49-51, 58, 60-63, 69, and 71-74.

Rejection Under 35 U.S.C. §112, First Paragraph

Claims 51, 58, and 60-63 are rejected under 35 U.S.C. §112, first paragraph, as being indefinite. The Examiner states that the recitation of the phrase "secondary disease manifestations" is not defined in the specification.

Independent claims 49, 58, and 69 have been amended to specify the nature of the "secondary disease manifestations" as "inflammation, fibrosis, induced auto-immunity and apoptosis and combinations thereof." This phrase is now clearly defined in claims 51, 58, and 60-63. Withdrawal of the rejection is respectfully requested.

Rejection Under 35 U.S.C. §102(b)

Claims 69 and 73 are rejected under 35 U.S.C. §102(b) as being anticipated by Yan et al., J. Can. Res. Clin. Oncol. 122:289-295 (1996). The Examiner states that Yan discloses that Tupaia can be experimentally infected with human hepatitis B virus (HBV) and that infection can be prevented by immunization with the hepatitis B vaccine.

Independent claim 69 has been amended to recite that the therapeutic method is carried out on the infected Tupaia. Thus, the present invention first creates an infection in the animal model and subsequently treats the infection. These steps are absent in the Yu reference.

To anticipate, a prior art reference "must disclose each and every feature of the claimed invention, either explicitly or inherently." MPEP § 2131; *Glaxo Inc. v. Novopharm Ltd.*, 52 F.3d 1043, 1047 (Fed. Cir. 1995). Yu clearly does not anticipate the rejected claims because Yu does not teach treating an infected subject. Withdrawal of the rejection is respectfully requested.

Conclusion

Applicants respectfully submit that all claims are in condition for allowance. Early notification of a favorable consideration is respectfully requested. In the event any issues remain, Applicants would appreciate the courtesy of a telephone call to their counsel at the number listed below to resolve such issues and place all claims in condition for allowance.

Respectfully submitted,

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